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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,481	11/01/2001	Qun-Yong Zhou	P-UC 5016	4599

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EXAMINER	
JIANG, DONG	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,481	ZHOU ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-90* is/are pending in the application.

4a) Of the above claim(s) *1-32 and 53-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-90* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5 IDSs*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's election with traverse of Group VI invention, claims 33-41, and 47-52, directed to SEQ ID NO:6, filed on 14 October 2003 is acknowledged. The traversal is with respect to the division of the claims of elected Group VI from those of Group V, and is on the ground(s) that a thorough search of Groups VI claims will identify art relevant to Group V, and although receptor antagonists and agonists identified using the claimed methods are expected to differ structurally, both methods result in identifying a compound altering production of a prokineticin receptor signal or prokineticin binding. This argument is persuasive, and the restriction requirement for Groups V and VI is withdrawn.

Applicants further traverse the "species" election requirement with respect to SEQ ID NO:3, 6, 13 and 14, in particular regarding SEQ ID NO:13 and 14 on the ground that each of SEQ ID NO:13 and 14 contain both a portion of SEQ ID NO:6 and a portion of SEQ ID NO:3 (chimeric), and therefore, a search of prior art in relation to SEQ ID NO:6 will reveal art relevant to SEQ ID NO:13 and 14. This is not found persuasive because a search is aimed to find references which would render the invention obvious, as well as references directed to anticipation of the invention. Therefore, a search for one group is not adequate as to revealing references anticipating the other groups. In the instant case, for example, a search of SEQ ID NO:6 (*the elected*) would not necessarily reveal *anticipating* information about SEQ ID NO:13 and 14 as they comprise additional sequences other than SEQ ID NO:6. Thus, independent searches are required for different SEQ ID NOs. Further, as applicants pointed out, the elected group of claims do not even recite SEQ ID NO:13 and 14.

Applicants are also reminded that the sequence election is not a species election, rather, it is a restriction requirement (see the last Office Action, paper No. 14, page 5, the last paragraph).

The requirement is still deemed proper and is therefore made FINAL.

Currently, claims 1-90 are pending, and claims 33-52 are under consideration. Claims 1-32 and 53-90 are withdrawn from further consideration as being drawn to a non-elected invention.

Formal Matters:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

Claim 48 is objected to for encompassing a non-elected subject matter, SEQ ID NO:3. The applicant is required to amend the claims to read only upon the elected invention.

Claims 36, 39, 44 and 50 recite specific a cell line, M2A7 (ATCC CRL-2500), but the specification does not provide the deposit statement indicating the deposit material will be readily available to the public without restriction upon issuance of the patent. However, as the cell line is known in the art, and readily available to the public, a rejection of the claims under 35 U.S.C. 112, first paragraph, for lack of enablement is not imposed.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33 is indefinite for the recitation of "said compound being characterized as a prokineticin receptor ligand". It is unclear what is the characteristic of a prokineticin receptor ligand, i.e., what method step is implied. The metes and bounds of the claim, therefore, cannot be determined. Claims 42 and 47 are similarly indefinite.

Claim 37 is indefinite because with the addition of a method step to further determine the ability of the ligand to agonize or antagonize said receptor signaling, it is unclear how and when it is determined, and what the result from such means. Claims 41, 46 and 52 are similarly indefinite.

The remaining claims are rejected for depending from an indefinite claim.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 33, 34, 37, 41, 42, 46-48 and 52 are rejected under 35 U.S.C. 102(e) as being anticipated by Sheppard et al. (US 6,485,938 B1, provided by applicants).

Sheppard discloses a human protein, Zven1, having an amino acid sequence of SEQ ID NO:2, which is 100% identical to SEQ ID NO:6 of the present invention (see appended computer printout of sequence search results).

Additionally, Sheppard teaches a two types of Zven analogs, a Zven agonist and a Zven antagonist; and a method of identifying such analogs as that a Zven agonist binds with a Zven receptor and stimulates a response by a cell expressing a Zven receptor, and a Zven antagonist that may diminish Zven agonist activity by a competitive or non-competitive binding of the antagonist to the Zven receptor (column 41, lines 5-17). Further, Sheppard teaches the detail regarding the method as that the activity of a Zven agonist or antagonist can be determined by assays well known in the art (references provided), and exemplifies testing a Zven polypeptide sample by measuring vasodilation of aortic rings (column 42, lines 18-51). Although the reference does not explicitly mention prokineticin (or Zven) receptor, or "specifically *binds* to said receptor" (as the present claim 33), they are an inherent property because Sheppard teaches that Zven polypeptides function through binding to a receptor, and the aortic rings used by Sheppared would necessarily have comprised the Zven receptor in order to respond upon Zven stimulation. As such, the reference anticipates claims 33, 37, 41, 42, 47 and 48

Further, Sheppard teaches that enhancement or relaxation of contractility by Zven polypeptides, their agonists and antagonists can be applied to contractile tissues such as gastrointestinal tissues (column 42, the second paragraph), and that, as an illustration, Zven antagonists can be used to inhibit contraction of the ileum (column 41, lines 57-58). Although Sheppard does not explicitly mention the term "an intestinal smooth muscle preparation" (as in

the present claim 34), "gastrointestinal tissues" or "the ileum" necessarily contain intestinal smooth muscle, and therefore, would meet the limitation of "an intestinal smooth muscle preparation". Therefore, the reference also anticipates claims 34, 46 and 52.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 35, 38, 43 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheppard et al. (US 6,485,938 B1), as applied to claims 33-35, 37, 38, 40-43, 45-49, 51 and 52.

The teachings of Sheppard are reviewed above. The primary reference does not explicitly and directly teach the method of identifying a prokineticin receptor ligand, wherein the preparation is a cell line or membrane preparation (as the present claims).

However, Sheppard teaches a method of identifying cells, tissues, or cell lines expressing a functional Zven receptor as that the activity of Zven can be measured by a silicon-based biosensor microphysiometer, which can be used to measure a variety of cellular responses, and to identify cells, tissues, or cell lines responding to a Zven stimulated pathway, and expressing a functional Zven receptor (column 43, lines 22-32, and the last paragraph).

Furthermore, Sheppard teaches that Zven, the agonists and the antagonists thereof are valuable in both in vivo and in vitro uses (column 41, lines 40-41), for example, Zven

polypeptide may be used in the treatment of disorders associated with gastrointestinal cell contractility, ... and Zven antagonists are useful for clinical conditions associated with gastrointestinal hypermotility such as diarrhea and Crohn's disease (column 55, the third paragraph), and can be used to inhibit contraction of the ileum (column 41, lines 55-59).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to identify a prokineticin receptor ligand ("Zven analogs") by measuring the activity of a Zven agonist or antagonist using assays well known in the art as suggested by Sheppard, and using the cells, tissues, or cell lines expressing a functional Zven receptor, identified by Sheppard's method. The person of ordinary skill in the art would have been motivated to identify a prokineticin receptor agonist or antagonist because they are valuable in both in vivo and in vitro uses including therapeutic applications as taught by Sheppard, and reasonably would have expected success because those cells, tissues, or cell lines taught by Sheppard express a functional Zven receptor.

Claims 40, 45 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheppard et al. (US 6,485,938 B1), as applied to claims 33-35, 37, 38, 40-43, 45-49, 51 and 52 above, in view of Costanzo (Physiology, Board Review Series, page 21, Williams & Wilkins, 1995).

The teachings of Sheppard are reviewed above. The primary reference does not explicitly teach the method of identifying a prokineticin receptor ligand, wherein the *Zven* ligand-receptor signaling is determined by monitoring *calcium* mobilization (as the present claims) even though Sheppard teaches that metabolic events that are often linked to receptor-ligand interaction include ..., mobilization of cellular calcium, ... (column 10, lines 58-61); and that the activity of a Zven agonist or antagonist can be determined by assays well known in the art (references provided), such as ... changes in ion channel influx, ... (column 41, the last paragraph to column 42, the first paragraph).

Costanzo teaches steps in excitation-contraction coupling in smooth muscle, including an increase in intracellular calcium levels (page 21, "B").

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to identify a prokineticin receptor ligand by monitoring the effect of the ligand on calcium mobilization because metabolic events that are often linked to receptor-ligand interaction include mobilization of cellular calcium, and that Zven is involved in contractility of tissues, such as gastrointestinal tissues (smooth muscle contraction) as taught by Sheppard, and because smooth muscle contraction involves calcium mobilization as taught by Costanzo. The person of ordinary skill in the art would have been motivated to identify a prokineticin receptor agonist or antagonist because they are valuable in both in vivo and in vitro uses including therapeutic applications as taught by Sheppard, and reasonably would have expected success because the assays for measuring calcium mobilization have been well-established in the art, and are widely practiced in the field.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

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AU1646
1/3/04